Identification and Targeting of Long-Term Tumor-Propagating Cells in Small Cell Lung Cancer.

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Public Summary:

Small cell lung cancer (SCLC) is a neuroendocrine subtype of lung cancer characterized by fast growth, early dissemination, and rapid resistance to chemotherapy. We identified a population of long-term tumor-propagating cells (TPCs) in a mouse model of SCLC. This population, marked by high levels of EpCAM and CD24, is also prevalent in human primary SCLC tumors. Murine SCLC TPCs are numerous and highly p roliferative but not intrinsically chemoresistant, indicating that not all the clinical features of SCLC are linked to TPCs. SCLC TPCs possess a distinct transcriptional profile compared to non-TPCs, including elevated MYC activity. Genetic and pharmacological inhibition of MYC in SCLC cells to non-TPC levels inhibits longterm propagation but not short-term growth. These studies identify a highly tumorigenic population of SCLC cells in mouse models, cell lines, and patient tumors, and a means to target them in this most fatal form of lung cancer.

Scientific Abstract:

Small cell lung cancer (SCLC) is a neuroendocrine lung cancer characterized by fast growth, early dissemination, and rapid resistance to chemotherapy. We identified a population of long-term tumor-propagating cells (TPCs) in a mouse model of SCLC. This population, marked by high levels of EpCAM and CD24, is also prevalent in human primary SCLC tumors. Murine SCLC TPCs are numerous and highly proliferative but not intrinsically chemoresistant, indicating that not all clinical features of SCLC are linked to TPCs. SCLC TPCs possess a distinct transcriptional profile compared to non-TPCs, including elevated MYC activity. Genetic and pharmacological inhibition of MYC in SCLC cells to non-TPC levels inhibits long-term propagation but not short-term growth. These studies identify a highly tumorigenic population of SCLC cells in mouse models, cell lines, and patient tumors and a means to target them in this most fatal form of lung cancer.

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